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PRESENT CONCEPTS IN INTERNAL MEDICINE. INFECTIOUS DISEASE SYMPO--ETC(U)
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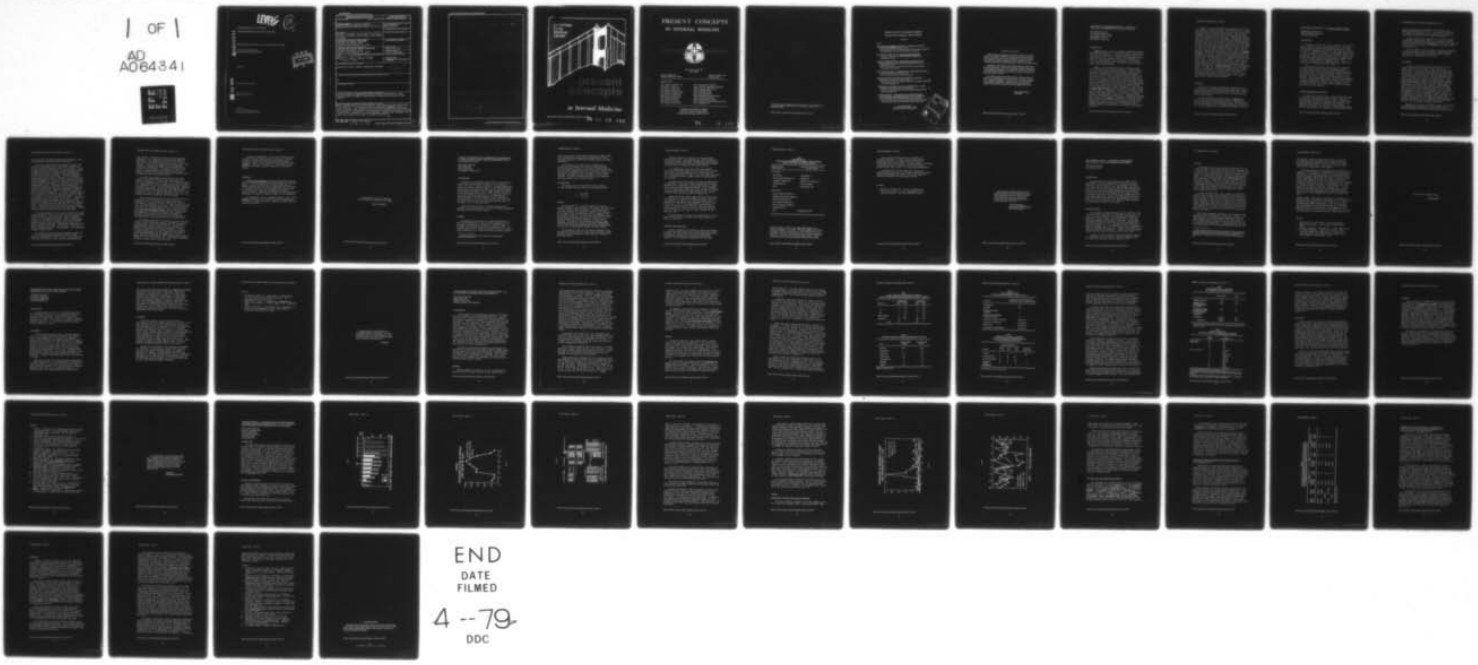

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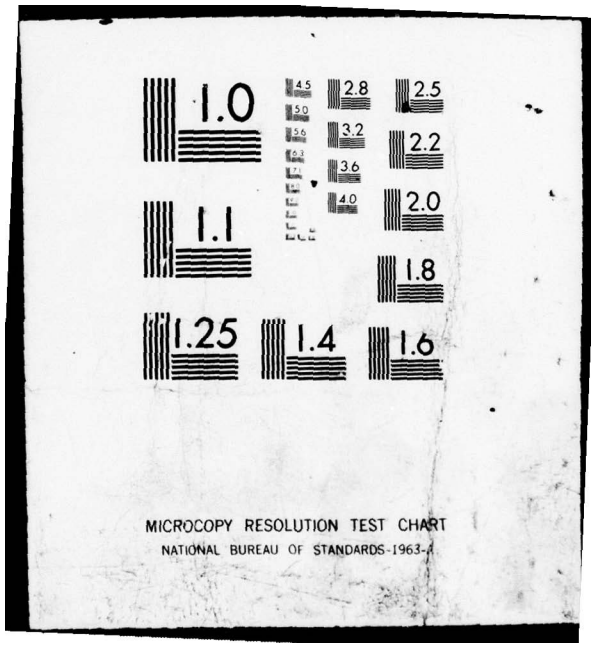
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INFECTIOUS DISEASE SYMPOSIUM

PRESENT CONCEPTS IN INTERNAL MEDICINE

COL Fred R. Stark, MC, Nina Z. Sanders, B.A., and Cathleen E. Swee, M.A.

Letterman Army Medical Center
Presidio of San Francisco, CA 94129

1978-1979

Infectious Disease Symposium

prepared for
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20. ABSTRACT *(Continue on reverse side if necessary and identify by block number)*

This symposium consists of seven articles, seven tables, and five figures (for quick reference). It includes articles on myocardial abscesses; zoster outbreak; anaerobic scalp abscesses related to scalp fetogram monitor electrodes; peritoneoscopy in aspiration of liver abscesses; staphylococcal disease and nasal carrier state; transmission of enteropathogenic organisms from Vietnamese children; and a report of two cases of candida peritonitis.

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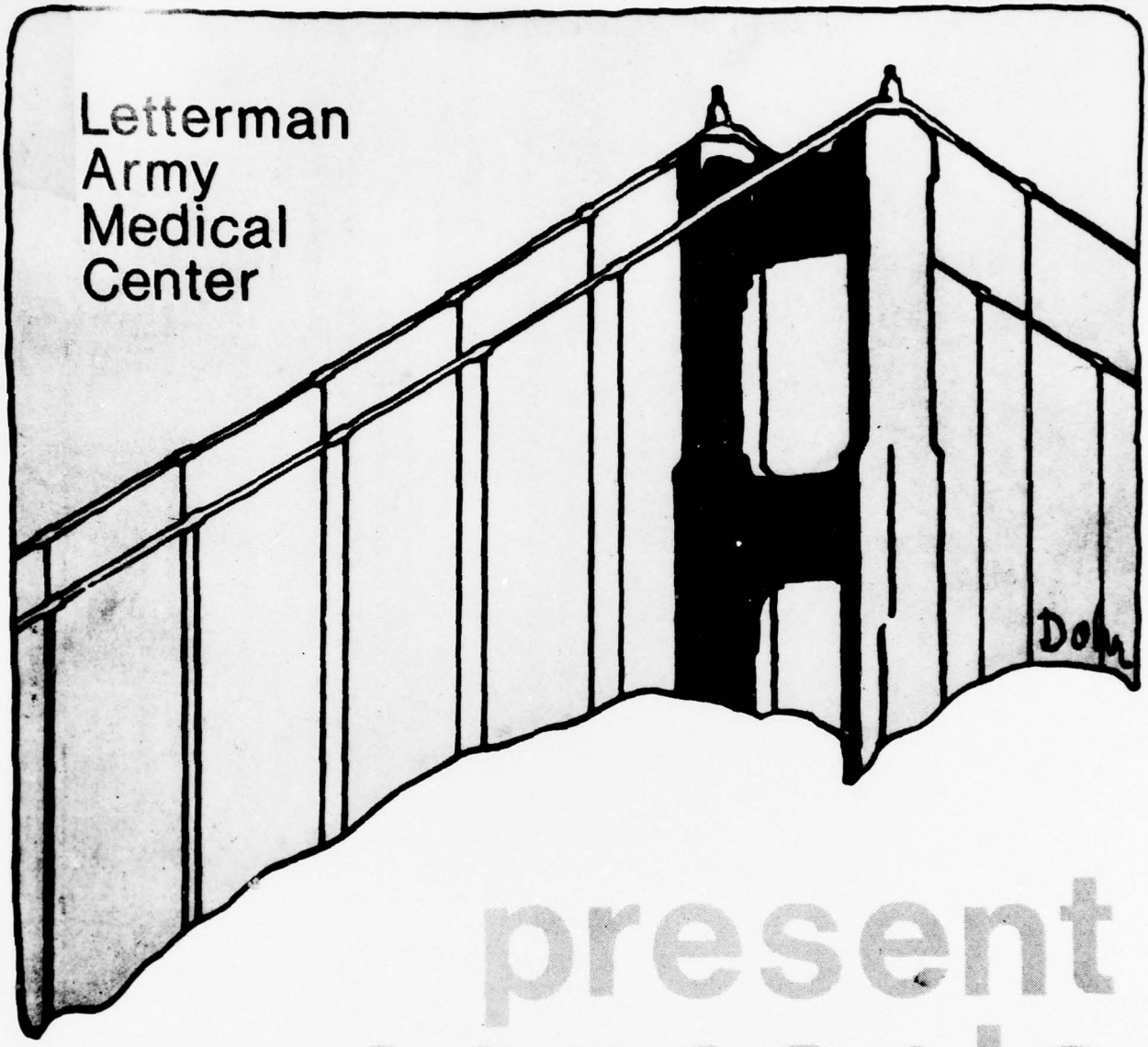

present concepts

in Internal Medicine

INFECTIOUS DISEASE SYMPOSIUM, WINTER 1978-1979

PRESENT CONCEPTS

IN INTERNAL MEDICINE

COL Fred R. Stark, MC
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Infectious Disease Symposium, Winter 1978-1979

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Present Concepts, Infectious Disease Symposium, Winter 1978-1979

PRESENT CONCEPTS IN INTERNAL MEDICINE

Infectious Disease Symposium, Winter 1978-1979

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DEDICATION

This brief issue is dedicated to the late Dr. Malcolm Artenstein, Walter Reed Institute of Research, great infectious disease scientist, teacher, and friend, and to his two colleagues, Drs. Jay Sanford and Louis Weinstein, who encouraged him in his establishment of the first Army Fellowship in Infectious Diseases with LTC Edmund Tramont.

The Editor of this edition of the ***Present Concepts*** is grateful for the wisdom, patience, and interest, during his training, of this group of fine scholars and teachers. It is hoped that these modest papers by the Editor and his students may honor Dr. Artenstein's memory and pique the interest of others.

Dr. Malcolm Artenstein trained in infectious diseases in Boston under Dr. Louis Weinstein in the Tufts Service. He is justly famous for his original contributions: the discovery of the German Measles virus and the development of a highly successful meningococcal vaccine which has saved thousands of lives throughout the world.

COL Fred R. Stark, MC
Guest Editor

CIMETIDINE AND CANDIDA PERITONITIS – REPORT OF TWO CASES FOLLOWING PERFORATED PEPTIC ULCER

COL Fred R. Stark, MC
LTC Nicholas P. Ninos, MC
COL John E. Hutton, Jr., MC
MAJ Ronald L. Katz, MC
LTC Melvin L. Butler, MC

INTRODUCTION

Candida peritonitis is an uncommon complication following bowel perforation. /1/ We saw two cases in one month and raise the question as to whether immune function is not impaired with cimetidine, a potent H2 blocking agent /2,3/ which in high doses produces some T cell dysfunction *in vitro* /4/, and whether T cell impairment or other white blood cell dysfunction leads to unusually poor clearance of yeast from the peritoneum.

Case 1: A 57-year-old man had a perforated peptic ulcer 72 hours after starting cimetidine. Shortly before the onset of abdominal pain and swelling, he had received penicillin and gentamicin for gram negative pneumonia. Free air was noted in the peritoneal cavity 24 hours after the onset of pain. During surgery, we noted a large duodenal ulcer perforation with bile-stained peritoneal fluid. After we accomplished primary closure and oversewing of the ulcer, we irrigated the peritoneal cavity with approximately 10 liters of crystalloid solution which included 50,000 units of bacitracin and 1 gram of kanamycin. A pure culture of Clostridium kruseii was grown from the peritoneal cavity. Ten days later, a temperature elevation to 40 C and increasing pain prompted reoperation. We drained an extensive abscess of the right upper quadrant which contained large numbers of pseudohyphae on gram stain. Culture again yielded pure culture of C. kruseii. Intravenous cimetidine, 300 mg every six hours, was administered from 3 to 10 days after perforation. Antibiotics in the postoperative period included clindamycin and amikacin in conventional doses. Amphotericin B 25 mg daily given for 14 days was associated with cure.

Case 2: A 72-year-old woman was hospitalized for fracture of the 5th lumbar vertebra. She had a history of pelvic adenocarcinoma of cervical origin that had been treated with irradiaton with no evidence of recurrence. The day after admission, pneumococcal meningitis was diagnosed and penicillin, 24 megaunits daily, was begun. Progressive abdominal pain and free air under the diaphragms were detected on the fifth hospital day. At surgery, we noted a large perforated duodenal ulcer and signs of early peritonitis. We oversewed the ulcer and irrigated the peritoneal cavity with 10 liters of Ringer's lactate and povidone-iodine solution. The wound was left open for delayed primary closure. Gram stain revealed no organism and cultures grew few colonies of Candida albicans. The patient was placed on intravenous cimetidine, 300 mg every 6 hours. On the seventh postoperative day, the patient was reoperated because of her persistent fever and leukocytosis. We discovered a left subhepatic abscess yielding 75 cc of a whitish glistening material. After noting large numbers of hyphal forms on the gram stain of the abscessed material, we placed drains and instituted amphotercin B irrigations. Candida albicans was the only organism grown. The wound was irrigated for three days with amphotercin B, followed by intravenous administration of amphotercin B, 20 mg daily, for three weeks. The patient defervesced slowly over a period of seven days, but died of neurologic complications of meningitis. At autopsy, there was no evidence of candidiasis.

DISCUSSION

Because our two patients required intensive care, no special studies of immune response were undertaken. Serum protein electrophoresis and total white blood cell counts and differentials were appropriate for the clinical condition in each patient.

We have identified only four cases of Candida peritonitis at Letterman Army Medical Center, including the two here reported, in the last seven years. The total number of cases reported in the English literature in 1976 was 34. We are impressed that, although many patients receive

MYOCARDIAL ABSCESS DUE TO LISTERIA MONOCYTOGENES

CPT Patrick J. Scannon, MC
CPT Christopher B. George, MC
COL Fred R. Stark, MC

INTRODUCTION

We report a patient with a rare infection in an unusual place, treated by a new, and probably superior, regimen, with excellent clinical and microbiologic results. Only 14 reports of Listeria infections of the heart were reported by 1975 /1/, and not one report of a myocardial abscess in an adult presenting as septicemia is available in the recent literature. Recent reports by Moellering /2/ suggest that marked penicillin-aminoglycoside synergism is demonstrable *in vitro* in most strains of Listeria tested. The occasional treatment failure noted with this organism may relate to its "enterococcus-like" behavior.

When six blood cultures positive for this organism were recovered from the blood of an elderly patient, antibiotic synergism was quickly demonstrated utilizing a new rapid method. Subsequent antibiotic therapy resulted in effective clinical and microbiologic control of the patient's infection. Because of associated severe heart disease, a fatal arrhythmia ensued, affording an opportunity to view the pathologic changes in the heart, after "cure." Although organisms were visible in small number in the abscesses, they were no longer viable, further confirming the success of the regimen.

METHODS AND LABORATORY RESULTS

In microtiter plastic plates, serial twofold dilutions of penicillin and gentamycin were arranged in classic "checkerboard" fashion by Microtiter, Inc. Several plates from the same lot used were compared with classical tube synergism and confirmed as accurate, using several enterococcal strains. An inoculum of 10^6 organisms per ml of final concentration was prepared in Mueller Hinton broth

using a calibrated loop inoculator of the Steers type, manufactured by Microliter, Inc. The inoculator was used to charge the microplate, and to subculture it on agar at four, eight, and 18 hours for bacterial estimates.

Marked (sixteen-fold) reduction in the blood minimum bactericidal concentration (MBC) for penicillin, from the 4 μg/ml to 0.25 μg/ml of the Listeria, and fifty-fold reduction (from 50 μg/ml to 1 μg/ml) for gentamycin was noted, using synergism plates.

With the addition to the regimen of gentamycin compared to penicillin alone, serial dilutions of peak and nadir sera from the treated patient revealed similar, marked synergism in conventional tube testing.

CASE REPORT

A 68-year-old Caucasian man was admitted for daily fever spikes of 37.8 C to 38.9 C (100 F to 102 F), weight loss of 3.6 kg (8 lbs) in one month, and diarrhea for one week. The patient had suffered three myocardial infarctions (in 1953, 1957, and 1963) and had been treated for stable angina for 20 years. His last admission (in August 1975) was for control of congestive heart failure and frequent premature ventricular contractions. Other medical problems, all inactive, included stable pulmonary granulomas (in 1950), kidney stones (in 1950), peptic ulcer disease (in 1958), gout (in 1970), hyperlipidemia type IV (in 1970), and fasting hyperglycemia (in 1975). The patient had long-term abnormal liver tests (in 1970), hepatomegaly (in 1973), and splenomegaly (in July 1975), all believed to be in part caused by ethanol ingestion. He ceased heavy cigarette smoking in 1953. One week prior to admission, on routine cardiology evaluation, the patient's hematocrit was 37, erythrocyte sedimentation rate (ESR) was 52 mm/hour and his weight was 62 kg (137 lbs). At that time, no diastolic murmurs were heard.

Medications on admission included digoxin 0.25 mg daily, Aldactone® (spironolactone) 25 mg three times a day, Lasix® (furosemide) 40 mg daily, quinidine sulfate 200 mg

every six hours, Benemid® (probenecid) 500 mg daily, and acetylsalicylic acid 600 mg every three hours.

On physical examination, the patient was alert and oriented. His height was 170 cm (68 ins), weight was 63.2 kg (139 lbs), temperature was 37.2 C (99.2 F), blood pressure in the supine positive was 140/60/0 with a pulse of 72/min, and his blood pressure while standing was 120/60/0 with a pulse of 80/min. Seborrheic dermatitis of the scalp and ears was present. An eye examination revealed mild atherosclerotic changes, but no evidence of embolic phenomena. He had poorly fitting partial dentures, severe periodontitis, and many carious teeth. Neck veins were distended at 30 degrees to 6 cm above clavicles with hepatojugular reflux. Numerous spider angiomata and bilateral gynecomastia were seen on chest examination but there was no cervical or axillary adenopathy. Bilateral basilar fine rales were present. Pulsus alternans was briefly present on admission. His point of maximal impulse was sustained in the left 5th intercostal space (L 5ICS) 3 cm lateral to the mid clavicular line (MCL). S_1 and S_2 were normal with a soft aortic second sound. A grade II/VI holosystolic murmur was present at the apex and a new grade I/VI high pitched late diastolic murmur was noted at the 2nd intercostal space (2 ICS) along the left sternal border. Carotid pulses had normal upstroke and bilateral bruits. Subclavian and femoral bruits were heard. Dorsalis pedis and posterior tibial pulses were diminished.

His liver measured 10 cm vertically overall in the MCL and was palpable 4 cm below the right cortical margin both in the MCL and the xyphoid process. Bowel sounds were normal. The genitalia were normal. Rectal examination revealed a 1 cm diameter prostatic nodule on an otherwise normal prostate. Stool was black and tar-like, and 4+ positive by Hemoccult® test. Dupuytren's contractures and early clubbing were present in both hands. There was no edema or cyanosis present. The remainder of the examination revealed normal results.

The patient's initial hemogram revealed a hematocrit of 27%, white blood cell count of 8.5 mm^3, platelet count of 225,000/mm^8 and ESR of 52 mm. Electrolytes and creatinine were normal. Both blood and fasting glucose

were 170 mg%. Urinalysis was normal without hematuria. Rheumatoid factor (Wampole) was negative and VDRL was nonreactive. Acid phosphatase was 0.44 IU/L (normal = 0.09 IU/L to 0.52 IU/L), alkaline phosphatase was 92 mu/ml (normal = 30 mu/ml to 50 mu/ml), and serum glutamic oxaloacetic transaminase (SGOT) was 132 mu/ml (normal = 15 mu/ml to 15-50 mu/ml). The remainder of SMA 12 was normal. Clotting studies were within normal limits. Salicylate level was 0.0 mg% one day after admission and digoxin level was within normal limits.

On chest roentgenogram, multiple small calcified nodules in the apex of the left lung were seen to be stable in comparison to prior films. His cardiac silhouette was enlarged overall with a lobular lateral contour on the left consistent with a left ventricular aneurysm. Pulmonary vasculature was normal. An electrocardiogram was abnormal, revealing regular sinus rhythm with first degree atrio-ventricular block, old anterior myocardial infarction and ST elevation in V_1 and V_2, and ST depression in V_4 to V_6. No changes were seen in comparison to old tracings.

Cautious transfusions of two units of packed red blood cells were given to the patient to correct his mild hypotension. The stools quickly became guaiac negative and hematocrit stabilized at 35%. The upper gastrointestinal tract and a barium enema were normal. Four initial aerobic blood cultures, positive within 24 hours, were identified as growing Listeria monocytogenes. The antibiogram showed the organism to be sensitive to ampicillin, cephalothin, chloramphenicol, colistin, erythromycin, gentamycin, kanamycin, minocycline, penicillin G, and tetracycline. The organism was intermediately sensitive to methicillin.

Intravenous penicillin G, 20 million units per day, was started. Based on synergism studies, gentamycin was added intramuscularly, 80 mg every eight hours. The patient became afebrile within 12 hours after institution of the penicillin G and remained afebrile thereafter. On the fifteenth hospital day, the prostatic nodule was biopsied for possible malignancy via the transperitoneal approach. Severe bleeding ensued from the biopsy site. Onset of angina and electrocardiographic (ECG) abnormalities prompted admission to the coronary care unit. Refractory ventricular arrhymias developed and the patient died.

Postmortem examination of the heart revealed an area of infarction and necrosis of the free wall of the left ventricle. Within the infarcted area multiple small abscesses yielded "B and B" positive rods consistent with Listeria. Cultures were negative. No evidence of endocarditis was noted on careful inspection of the heart valves.

DISCUSSION

Listeria monocytogenes, an occasional isolate from the mouth in normal persons, may become an invader via diseased gingiva. In this patient with a recent infarction, it appears possible that the area of hemorrhage and infarction, or the subjacent area of fibrin deposition, became a site for seeding of the organism, and sepsis and abscess formation ensued. There was no evidence from the postmortem examination to support a valvular origin of the infarction.

We recommend the use of synergism studies in all serious Listeria infections. We believe the "micro-checkerboard" technique to be accurate and far simpler to perform than the conventional method.

I would rather be a servant in the house
of the Lord than sit in the seats of the mighty.

– **Senator Alben Barkley**

VARICELLA SUPERINFECTION: EPIDEMIOLOGIC EVIDENCE FOR A ZOSTER OUTBREAK AMONG IMMUNOCOMPROMISED ADULTS IN AN ONCOLOGY CLINIC

COL Fred R. Stark, MC
Terry Collins, RN
Glen R. Justice, MD
COL Eugene P. Flannery, MC

INTRODUCTION

Herpes zoster represents reactivation of varicella in persons who have diminished immunity. /1/ Clusters of zoster cases occur in cancer centers.* We have studied the nature of zoster-to-zoster exposure in 11 immunocompromised persons who contacted herpes zoster in the oncology clinic at Letterman Army Medical Center (LAMC) during a two-month period and compared them with 71 other patients treated in the clinic during the same period. We concluded that immunocompromised patients who have intimate exposure to zoster patients, e.g., from sitting in the same chair used by zoster patients while receiving chemotherapy, have an increased risk of obtaining zoster.

Since the application of a control program in the oncology clinic, the incidence of zoster in immunocompromised patients has substantially declined.

METHODS

We diagnosed herpes zoster on clinical grounds as a varicelliform eruption in one or several dermatomic sites. Serologic confirmation was obtained in doubtful cases. Cultures for varicella virus were not routinely done. We obtained routine viral cultures from many lesions to exclude herpes hominis virus. Culture material was usually placed

*Personal communication from Dr. Thomas Merigan, Chief, Infectious Disease, Stanford University, Stanford, CA.

directly on tissue culture media African green monkey HeLa cells (kidney) and transported for implantation to the Reference Laboratory, Sixth United States Army, Fort Baker, California.

All patients with herpes zoster diagnosed from January 1975 to February 1976 and all control patients were interviewed in detail by the staff, Infection Control Service, LAMC, regarding history of varicella, zoster, time and place of oncology visits, and exposure to varicella, children (in a home or school setting), or other zoster patients. Details of the medical history were obtained from the patients and by record reviews.

Statistical Analyses

Chi square tests of significance were performed for all the above factors using the following equation:

$$X = \frac{(a - rb^2)}{r\,(a + b)}$$

RESULTS

We analyzed 61 of 71 control records of oncology patients treated in the oncology clinic, LAMC. We found that 35 of the persons with no evidence of zoster during the previous 12 months were exposed to patients with zoster in the oncology clinic from September 1975 to November 1975. The records of eight of the 11 persons who developed zoster during this period were available for evaluation. All of these patients had definite exposure to other zoster patients. The nature of the exposure in seven of eight instances consisted of sitting in the same "chemotherapy chair" where intravenous medications had been administered the same day an index zoster patient had been treated.

The probability that 35 of 61 persons exposed in the non-zoster group differed by chance from the eight of eight exposed in the zoster group is less than one in forty (p less than 0.025).

Measures employed to institute a control program included admitting to the hospital and isolating patients with active zoster, thoroughly cleaning and re-covering the chemotherapy chair after each use, and reducing the number of clinic visits of patients with active zoster.

In a population of this size (71), the expected zoster rate from data found in the literature and from our own experience is approximately four to six cases per year. The probability of eight of 10 zoster cases occurring in a three-month period by chance alone is approximately one in eight.

In the two-year period after the outbreak (1976-1977), we maintained a total surveillance program, with a slowly enlarged clinic population. During this period, we noted seven cases of zoster among 185 persons, for an incidence of 3.8%, compared with the attack rate of eight of 43 known exposed persons during the study period for an incidence of 18.5%. This difference again is significant.

Comparison of the control group with the zoster group by frequency of chemotherapy, stage of disease, age, sex, and frequency of visits to the oncology service clinic suggests that the groups were comparable in terms of risk of exposure. Five of the eight zoster patients gave a history of chicken pox in childhood. None was aware of recent exposure to children or active varicella patients. The adult oncology unit does not treat children in the same care area.

The distribution of disease and chemotherapy or other cancer therapy among the zoster and control patients is shown in the Table.

DISCUSSION AND CONCLUSION

A level of immunity low enough to permit reactivation of latent varicella virus exists in many oncology patients, especially in those patients receiving chemotherapy. It is commonplace nowadays to treat many such patients together. Is the notorious infectivity of the active

TABLE
DISTRIBUTION OF
DISEASE AND CHEMOTHERAPY (OR OTHER CANCER THERAPY)
AMONG THE ZOSTER AND CONTROL PATIENTS

Distribution of Disease *(Number of Patients)*	Chemotherapy (Or Other Cancer Therapy) *(Number of Patients)*
Zoster Patients	
Carcinoma *(4)*	Chemotherapy *(3)*
Chronic lymphocytic leukemia *(2)*	Prednisone *(1)*
Lymphocytic lymphoma *(1)*	Adriamycin and bleomycin *(1)*
Lymphosarcoma *(1)*	No current therapy
Total	Chemotherapy *(5/8)*
Control Patients	
Chronic lymphocytic leukemia *(11)*	
Hodgkin's disease (assorted stages) *(23)*	
Lymphocytic lymphoma *(15)*	
Acute lymphocytic leukemia *(3)*	
Chronic myelogenous leukemia *(3)*	
Lymphosarcoma *(6)*	
Total	Chemotherapy *(44/61)*

zoster patient a risk to the immunocompromised, but "varicella-immune," patient? Our data suggest a fivefold increase in risk in our clinic (3.8% versus 18.5%) over a three-year period of observation, and, during an apparent outbreak, of a 100% versus 61% exposure rate of zoster versus non-zoster cancer patients visiting the clinic.

Can varicella rechallenge produce disease in a localized dermatome? In mice, certain experimental rechallenge herpes virus infections will recur as a dermatomic form of the disease. In human beings, a challenge via an unusual route (accidental skin or intravenous exposure) may express zoster in a dermatome distribution.

We believe that further study will confirm our present observations that close patient-to-patient exposure among immunocompromised patients with zoster leads to increased infection risk in exposed patients.

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Often too great a concern is placed on the statistical aspects of data and experimental design. All the great discoveries of my lifetime required only a microscope, a test tube, and anyone without a day of mathematical training could see the importance of the work.

– **COL Edward Buescher**
(Mentor of Dr. Malcolm Artenstein at Walter Reed Institute)

THE "BERKELEY BARB" – ANAEROBIC SCALP ABSCESSES RELATED TO SCALP FETOGRAM MONITOR ELECTRODE

COL Fred R. Stark, MC
LTC Frank Crast, MC

INTRODUCTION

Accepted practice in obstetrics now includes routine monitoring of the fetal electrocardiogram via electrodes attached to the fetal scalp. /1/ An acceptably low infection rate with the original coil type electrode (approximately 0.3%) /2/ and fewer scalp contusions than with the older clamp type coil have prompted introduction of new designs. Routine total hospital surveillance of infections has been in effect at Letterman Army Medical Center (LAMC) since 1971. This study compares the rates of nonstaphylococcal neonatal scalp infections before and after the introduction in July 1974 of a new coil electrode, the "Berkeley Barb" (Berkeley Bio-Engineering, Berkeley, California).

METHODS OF STUDY

All records of maternal complications at LAMC for a two-year period (1973 and 1974) were surveyed and served as controls for rates of maternal infection and fever, perineal laceration, infant trauma, use of antibiotics, fetal scalp blood gas sampling, and patterns of delivery. Two hundred additional records of normal deliveries were combined with the above records to compare type and duration of delivery, hours of premature rupture of membranes, types of presentation, number of monitors and scalp blood samples, and patterns of obstetric training and methods of patients in two time frames: January 1973 to June 1974 and July 1974 to July 1975.

A review of scalp electrode placement showed no changes in technique in the two periods. Most staff members were not aware that they were using a different coil.

RESULTS

Nonstaphylococcal scalp electrode infections were recorded in seven of 300 infants delivered from September 1974 to January 1975. Five infections were severe; none was fatal. Six of the seven infections were caused by organisms which appeared as small gram negative, pleomorphic rods on gram stain. In two of the six infections, Bacteroides species were isolated after appropriate measures for anaerobic cultures were taken. In one case, no gram stain or positive culture was obtained. Six of the seven abscesses occurred in neonates who had been monitored by the new coil device. In the single case without coil monitoring, the neonate had a large scalp hematoma, and the mother had a postpartum temperature of 39 C.

Duration of monitoring, labor, rupture of membranes, parity, fetal distress, type of delivery and presentation, and percentage of deliveries monitored did not differ between the early control period and the period of increased scalp infections. There was no change in rate of maternal fevers, postpartum infections, or frequency of fetal scalp blood samples for blood gas determinations between January 1973 and July 1975. Rates of coil monitoring of the fetus were 52% for the early period and 54% for the late period (after July 1974).

Six factors suggested association with neonatal scalp abscesses and were subjected to statistical analyses: the association with (1) fourth degree laceration; (2) blood scalp samples; and (3) monitored-to-unmonitored babies in the epidemic period, which was in all cases strong, but not statistically significant.* Comparison of (4) control-to-epidemic period, (5) old-to-new monitoring devices, and

*Method of P. Armitage, *Statistical Methods of Research*, example 4.13, page 140, Oxford 1971, performed by Alfred Allen, M.D., Director of Dermatological Research, Letterman Army Institute of Research, Presidio of San Francisco, California. The p values were: (1) greater than .10; (2) greater than .10; (3) greater than .10; (4) less than .001; (5) less than .002, and (6) less than .001.

(6) maternal infections suggested increased association with neonatal scalp infection when the new coil monitor was used during the epidemic period, especially in women with puerperal infections. The p values were less than .002 for the latter three relationships.

From this analysis, we concluded that two factors are related to the prevalence of nonstaphylococcal neonatal scalp infections: (1) maternal infection with transient sepsis, possibly related to perineal injury, and (2) neonatal scalp trauma, apparently more severe or located in a more susceptible tissue plane of the scalp with use of the newer, larger coil monitoring device, the "Berkeley Barb." Although the numbers are small and open to some question, the trend is striking enough to provoke us to discontinue use of the larger coil in favor of the older, smaller coil. A scalp infection rate 28 times higher than we previously experienced, and 10 times higher than our published experience, constrains us from recommending the use of the larger barb coil.

(EDITOR'S NOTE: This report, forwarded to the Center for Disease Control, was extended and published by our Obstetrics and Gynecology Department as a full report. /3/ In the following year (1976), manufacture of the "Berkeley Barb" was discontinued in favor of smaller devices. Currently, infection rates for scalp monitors remain above the old, published rate of 0.3%, and are in the range of 1%, but are still far below that listed during the "Berkeley Barb" era.)

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There is no virtue without courage.

– **Winston Churchill**

PERITONEOSCOPY IN THE ASPIRATION OF MULTIPLE AMOEBIC ABSCESSES OF THE LIVER: A CASE REPORT

COL Fred R. Stark, MC
LTC Melvin L. Butler, MC
LTC David C. Staples, MC
CPT Paul Bergfelder, MC

INTRODUCTION

No reports exist on the use of peritoneoscopy with directed needle aspiration as an alternative approach to the large amoebic abscess. The only mention of this approach is a single brief comment in a review article on laparoscopy in 1977. /1/ We report a favorable, convenient method of approach to two large abscesses in the right and left lobes of the liver.

CASE REPORT

A 21-year-old man returned from a two-week camping trip in the northern California foothills complaining of fever, vague abdominal pain, headache, and weakness. Doxycycline, 200 mg/day, was begun and his fever promptly declined from 40 C to 37.7 C (104 F to 100 F) in a 48-hour period. Five days later, he had a fever of 38.9 C (102 F) and pain in the right upper quadrant and in the right pleura, and he was extremely weak. A liver-spleen scan revealed two large defects of the liver. Treatment with metronidazole, 750 mg three times a days, was begun. After seven days of therapy, the fever persisted and the pain worsened. A repeat liver-spleen scan at that time revealed no change.

Emetine was added and peritoneoscopy was performed on the tenth hospital day. Via peritoneoscopic visualization, a separate needle was directed into each abscess using a right subcostal approach to the right lobe and a subxyphoid approach to the left lobe. Approximately 300 cc of "anchovy paste" were removed from the left abscess and

100 cc from the right abscess which on examination contained many white blood cells and no organisms. Emetine was continued for an additional 10 days, after which the patient was released from the hospital. A three-month follow-up scan revealed a marked (90%) decrease in the size of the abscesses and a well patient. Laboratory data confirming the diagnosis included a latex slide test and a positive hemagglutination inhibitor test for amebiasis. Further history from the patient revealed that he had taken a trip to Mexico four months prior to admission during which time he had a five-day episode of unexplained fever and diarrhea.

DISCUSSION

Favorable reports on the use of percutaneous aspiration of an hepatic amoebic abscess are recorded. /2,3/ When the lesion is on the left side and near the dome of the diaphragm, however, a substantial risk of complication exists, and surgical intervention, with its attendant morbidity and mortality, may be required. In the present case, a lower, sharply angled approach was performed with the needle directed to the left lobe via the path used for pericardiocentesis. Likewise, because of the proximity of the abscess on the right lobe to the dome of the diaphragm, a similar oblique approach also was used. This approach, necessary for high lesions close to the dome, would be extremely hazardous without visual control.

Because of the success of this approach we recommend it especially for high hepatic lesions of the right or left lobe that require drainage because of failure of response to treatment, or size (greater than 10 cm) at presentation. We would presume that in the toxic individual presenting with a large abscess, peritoneoscopy would be far safer than general surgery, and far more reliable and accurate than blind percutaneous drainage.

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Young workers in a field may pine for "the simpler problems of yesterday." The future is opaque in science, as in everything else. There is no greater time to be alive in science than right now, but only the future will prove it.

– Anonymous

STAPHYLOCOCCAL DISEASE AND NASAL CARRIER STATE: USE OF ANTIBIOTICS AND RESISTANCE TO METHICILLIN

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INTRODUCTION

Certain aspects of staphylococcal disease in the United States vary greatly from the European experience. Serious infections due to methicillin-resistant (met-R) organisms are common in hospitals in Denmark /1/, Switzerland /2/, and England /3/. The evolution of these organisms from multiple resistant (mult-R) phage group III staphylococci has been proposed. /1/ In contrast, Sherris /4/ has presented evidence suggesting a decline in mult-R staphylococci and the near absence of met-R strains in the United States. Data are unavailable regarding the precise role of antibiotics in the selection of mult-R and met-R organisms. Surveys conducted in Denmark and United States show consumption of rather large quantities of tetracycline, streptomycin, and macrolide antibiotics over the last decade, as well as increased use of beta-lactose resistant (BLR) penicillins and cephalosporins. The prevalence of met-R strains in the United States, however, has not increased concomitantly.

Although the cephalosporin antibiotics have been used extensively at Walter Reed Army Medical Center (WRAMC) during the past decade, the use of BLR penicillins, tetracyclines, streptomycin, and erythromycin has declined. These studies were undertaken to assess more precisely the use of antibiotics, and to document the prevalence of mult-R and met-R staphylococcal strains at WRAMC.

METHODS

Using the methods of White et al /6/, we obtained and quantitated nasal cultures, plated them on mannitol salt,

and performed routine identification procedures, including gram stain, slide, and tube coagulase. Only "significant" colonizations, i.e., greater than 10^3 organisms per swab, were recorded as positive. Clinical isolates were obtained from the Microbiology Laboratory, WRAMC, and confirmed by the above methods. We performed antibiotic sensitivity assays using the Kirby-Bauer (K-B) single disc diffusion method. /7/ We also performed a plate dilution technique for methicillin on all organisms presumed to be met-R by K-B, and carried out incubation at 30 C. For BLR antibiotics, we used incubation at 30 C, standard K-B technique, and zone-size interpretation according to Sherris' method. /8/ A series of surveillance tests in April, May, and June 1972 and December 1972 through February 1973, conducted in all areas of the hospital except a few specialty services, yielded estimates of frequency of antibiotic use, categories of patients receiving antibiotics, and the frequency of nasal staphylococcal presence. From August 1973 to February 1974, we surveyed intensively a surgical suite of 70 beds in the renal transplantation and renal dialysis areas, including taking frequent nasal cultures of all patients and ward personnel.

From August 1972 to May 1973, the study physicians, preventive medicine officer, and a nurse epidemiologist surveyed the entire hospital for nosocomial infections. Their data provide the frequency of occurrence of nosocomial staphylococcal infections during the study period, as well as basic demographic information.

We calculated antibiotic use by the number of patients receiving a specific agent during a 24-hour period. In most instances, bedside records were surveyed for five to seven days and the use-prevalence (percentage of patients on drug/day) was calculated from the average.

Phage typing was accomplished in our laboratory following procedures outlined by Blair /9/, using phage and reference strains from the Center for Disease Control (CDC) and our own collection. Phage group I consists of phages 29, 52, 52A, 80, and 81. Phage group II consists of 3A, 3B, 3B, and 5C. Phage group III consists of 6, 7, 42D, 42E, 47, 53, 54, 71, 75, 77, 79, 83A, 84, 85, and 88. Other groups conconsist of WHI, D11, UC 18, WR 70, and 187. A phage

related to WHI, but with a somewhat different host susceptibility range and designated WR-70, was isolated from an organism recovered from a patient on the renal transplantation service. A total of 16 clinical isolates, eight of which were typable by WHI, were lysed by this phage under standard conditions. All of these organisms were pen-R, but were otherwise generally sensitive to other antibiotics. Methicillin resistance could not be induced by serial passage of these strains.

We employed a phage adsorption technique to study the surface phage binding sites on strains of met-R Staphylococcus aureus. In brief, 6 x 10^8 staphylococci, heat-killed (70 C for 15 minutes), were added to a solution containing 10^4 x RTD phage for 60 minutes at 30 C, and then removed by centrifugation. The supernatant containing unadsorbed phage was compared with a control (Staphylococcus epidermidis-adsorbed phage) for its titer against a susceptible organism. A two-log decrease in titer from control titer was considered to be a positive adsorption. The WRAMC strains were compared to 12 met-R strains, a gift from Dr. Leon Sabath, Boston City Hospital.

RESULTS

During the six-month study (August 1972 to January 1973), 8,982 patients were admitted to the survey area. Length of patient stay varied widely among the 21 patient care areas, but averaged about eight days. Twenty percent of patients in the study area had malignancies and were undergoing surgery, irradiation, or chemotherapy. Also included in the study were an active renal dialysis and renal transplantation program, the orthopaedic and general surgery services, all intensive care areas, and the entire medical service.

The total number of hospital-acquired Staphylococcus aureus infections during the six-month period was 89, including eight bacteremias. Data were available on the organisms of 52 of these infections. Distribution of phage types in these strains is compared with 150 strains from a hospital-wide carrier survey conducted during the same

period (Table 1). All major phage groups were represented in approximately equal proportions in the clinical isolates. Nontypable strains accounted for 45% of nasal isolates, the remaining strains being divided equally among the defined phage groups.

Antibiotic sensitivity studies are shown in Table 2. Patterns of resistance were similar in clinical and carrier strains with two exceptions: streptomycin and methicillin resistance was found only in carrier strains. Multiple resistant strains occurred in a total of 16 strains, which fell into phage groups III, WHI-WR70, or nontypable. The four met-R strains were also resistant to cephalosporin and were nontypable with the phages used. Twenty-five percent of all strains tested were resistant to novobiocin as were two of the four met-R strains. All staphylococci tested were sensitive to vancomycin, gentamycin, and tobramycin.

These data may be contrasted with those of Bulow /1/ in Denmark. In those studies, 60% to 80% of phage group III organisms were mult-R, whereas in our studies, 22% of phage group III strains were mult-R. Antibiotic use data are shown in Table 3. Cephalosporins and penicillins were being administered to 10% and 8% of hospital patients, respectively, and gentamycin to 5.4%. Erythromycin and tetracyclines were used in less than 0.5% of patients. Other published data in the United States /9,10,11/ suggest that our patterns of antibiotic use are similar, except for our rather high rate of cephalosporin use. Other medical centers in United States report a higher use of tetracycline and erythromycin. The current data show a much lower use of some of the "priming" antibiotics (tetracycline, erythromycin, streptomycin), to which many strains of staphylococci develop rapid resistance, than was noted by Bulow during the period of rising met-R staphylococcal disease in Denmark. /2/

Table 4 shows the relationship between hospital stay and antibiotic use, and resistance to penicillin, on a 70-bed surgical ward over a six-month period. In this hospital area, as in all others, staphylococcal carriage was sharply reduced in patients receiving cephalosporins. Penicillin resistance rose sharply with increased duration of hospital stay. On the surgical ward, a higher than expected incidence

TABLE 1

PHAGE TYPING OF STAPHYLOCOCCAL STRAINS
ISOLATED FROM NOSOCOMIAL INFECTIONS AND NASAL CARRIERS

	Clinical Isolates		Nasal Isolates	
Phage Group	Number	Percent	Number	Percent
I	14	26.4	16	10.6
II	5	9.4	24	16.0
III	9	17.0	21	14.0
WHI and WR-70	13	24.5	21	14.0
Nontypable	12	22.6	68	45.4
Total	53		150	

TABLE 2

ANTIBIOTIC RESISTANCE AMONG STAPHYLOCOCCAL ISOLATES

Drug	53 Clinical Isolates % Resistant	168 Nasal Isolates % Resistant
Penicillin	87.0	85.0
Streptomycin	0	13.6
Tetracycline	5.7	13.1
Erythromycin	3.8	9.5
Chloramphenicol	1.9	0.6
Methicillin	0	2.4
Mult-R*	9.4	6.6

*Mult-R = PT, PTE, PE, or PC

TABLE 3

USE OF ANTIBIOTICS AT
WALTER REED ARMY MEDICAL CENTER, 1972-1973

Antibiotics	Percentage of Total Patients Receiving Drug During 24-Hour Period (1050 Patients Surveyed)
Cephalosporins	10.2
Penicillins	8.1
Beta-lactamase resistant penicillins	2.7
Gentamycin (in combination with above antibiotics)	5.4
Streptomycin, neomycin, kanamycin	Less than 2.0
Lincomycin and clindamycin	Less than 2.0
Erythromycin	Less than 0.5
Tetracycline and chloramphenicol	Less than 0.5

TABLE 4

STAPHYLOCOCCAL NASAL CARRIERS
AS RELATED TO LENGTH OF HOSPITALIZATION
IN "HIGH CEPHALEXIN-USE WARD"*

Category	Period of Hospital Stay			Overall Carrier Prevalence (%)
	48 Hours or Less	2 to 14 Days	15 Days or More	
% carriers	51	11	9	20.1
% proportion Pen-R	48	80	100	
% proportion Mult-R	20	27	28	
% of patients receiving cephalosporins	20	38	28	2.8

* Six-month survey, 180 positive nasal cultures

of mult-R staphylococci was cultured on patient admission. This may be partially explained by the large number of elderly male patients who were transferred from a soldiers' home or hospital where use of antibiotics, particularly tetracycline and erythromycin, is liberal for treatment of chronic pulmonary disease and urinary tract infections.

A second "high risk" area (nosocomial staphylococcal infection rate was 9.3%) was also surveyed for nasal carrier state and antibiotic use over a three-month period. Staphylococcal disease occurred in four of 43 patients on the renal dialysis and transplantation ward; three of four were phage group III. Nasal carrier state averaged 35%, of which 26% were phage group III. In both areas, use of tetracycline, erythromycin, and streptomycin, antibiotics which are associated with emergence of mult-R in staphylococcus, was low (0.5%). In the same areas, phage group III organisms (precursors of met-R strains, according to Bulow /1/), were commonly isolated (averaging 15% of carriers) and use of beta-lactase resistant penicillin was high. Thus, in both areas, the important missing factor needed for the emergence of clinically significant met-R staphylococci was the use of "priming" antibiotics.

The relationship of nasal carrier state to concurrent antibiotic therapy is tabulated in Table 5. Less than 6% of patients receiving cephalosporins were carriers; similar data were noted years ago for BLR penicillins by Leedom et al /12/ The low carrier rate among patients treated with cephalosporin may be a major factor in the slow spread of mult-R strains in our hospital by eliminating a major group of prospective carriers. That is, many of the patients treated with the cephalosporins were seriously ill, often with staphylococcal infections, had wounds, or other jeopardized tissues likely to be sites of nosocomial staphylococcal infections. The phage group patterns among the treatment groups did not differ significantly. We did not have sufficient data on patients treated with BLR penicillins to comment on nasal staphylococcal carriage in that group.

Methicillin-resistant staphylococci were isolated from nasal swabs of four patients in adjacent beds on a surgical service during a two-week period. Careful observation failed to reveal evidence of met-R disease. The four strains were

TABLE 5

NASAL STAPHYLOCOCCAL CARRIERS*
BY ANTIBIOTIC USE AND PHAGE TYPE

	Number Positive	Percent
Cephalosporin therapy	4/68	5.9
Penicillin therapy (including methicillin and oxacillin)	16/56	28.5
Gentamycin (excluding those patients treated wtih other drugs in combination)	8/29	27.6
No antibiotics	112/429	26.1
Total Patients	150/602	24.9

*During this period staphylococcal disease rate was 1.0%. Ward personnel nasal staphylococcal carrier rate was 24.1%.

TABLE 6

CHARACTERISTICS OF
METHICILLIN-RESISTANT STAPHYLOCOCCUS AUREUS

	Strain Number	Phage Adsorption Pattern*
Walter Reed Army Medical Center †	23	88/75
	30	88
	72	88
	85	88/75
Boston City Hospital ‡	1	Not done
	2	88/81
	3	88/81/53/84
	6	88/81/53
	7	88/81/53
	8	88/81/84
	9	88/81
	10	88/81
	11	88/81/84

* The following phages failed to adsorb: 55, WHI, D11, 85, and 77.
† Strain numbers 23 and 85 had the following antibiotic resistance: PSETM, NB, Ceph. Strain numbers 30 and 72 had the following antibiotic resistance: PSETM, Ceph. All phage types were nontypable.
‡ All strain numbers had the following antibiotic resistance: PSETM, NB, Ceph. All phage types were nontypable, except for strain number 1 which was 29/85 (84,88).

broadly resistant to antibiotics and did not lyse with any of the full set of typing phages, but had the capacity to adsorb phages 88 and 75 (two strains), and failed to adsorb group I phages or WHI and D11. Table 6 shows their contrast with several met-R strains from Boston City Hospital which, in addition to phage 88, were also able to adsorb certain group I phages. These data suggest a common origin of the Walter Reed met-R strains and a minor difference from the Boston strains. Thus, the phage adsorption technique may be useful in epidemiologic studies involving nontypable staphylococci.

CONCLUSION

Nasal carrier state surveys, combined with antibiotic sensitivity studies and phage typing of staphylococcal isolates, suggest that phage group III carriage and disease is relatively common at WRAMC, although met-R strains have not emerged as a nosocomial infection problem. We specifically propose the theory implicit in the data of Bulow /1/: that environmental pressure on staphylococci to acquire met-R must include sufficient exposure to "priming" antibiotics before and after the introduction of BLR antibiotics. We believe this pressure may be generally absent in many acute care areas in hospitals in the United States, despite published data on use of antibiotics. With the introduction of the cephalosporin antibiotics in our acute care areas nine years ago, such "priming" antibiotics as tetracycline, the macrolides, and streptomycin have been used less frequently.

Saito et al /13/ have demonstrated that identical modes of action and mechanisms of resistance exist among the macrolides and macrolide-like drugs such as lincomycin and 7-chlorolincomycin. If this is the case, and given the increasing popularity of these new antibiotics as treatment for a wide variety of gram-positive and gram-negative bacterial infections, we predict the "priming" of currently prevalent staphylococci (perhaps phage group III) to mult-R antibiotics including met-R.

SUMMARY

Intensive surveys at WRAMC revealed rare nasal carrier isolates of met-R Staphylococcus aureus, and none from clinical isolates. An analysis of antibiotic use demonstrated infrequent administration of those antibiotics associated with mult-R ("priming") in staphylococci, i.e., tetracycline, erythromycin, and streptomycin, and high use of the cephalosporins. Cephalosporin administration was associated with markedly reduced nasal staphylococcal carriage. While phage group III organisms were present and caused disease, only 20% were mult-R and none were met-R. The phage adsorption patterns of the few met-R strains isolated suggested phage group III origin; the phage adsorption patterns were somewhat different from those of met-R isolates from Boston City Hospital. Phage adsorption is suggested as a possible method of analyzing otherwise nontypable met-R isolates.

The thesis is advanced that "priming" antibiotics are, in fact, infrequently used in epidemiologically important patients in acute care areas in the United States where BLR antibiotics are used extensively. However, growing popularity and use of such agents as lincomycin, 7-chlorolincomycin and newer tetracyclines may precipitate mult-R in staphylococci, thereby "priming" phage group III organisms to conversion to the met-R state.

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The epidemiology of some diseases gives them away. Long before the etiology of childbed fever was established, before Koch's postulates were fulfilled, workers became aware of the transmissable nature of childbed fever. In diseases such as cancer, epidemiological information, including genetic and environmental data, has not been fully exploited.

– **Daniel Thor**
Contemporary immunologist

"REVERSE TURISTA": TRANSMISSION OF ENTEROPATHOGENIC ORGANISMS FROM VIETNAMESE CHILDREN TO SAN FRANCISCO STAFF IN THREE TYPES OF EMERGENCY CARE FACILITIES

COL Fred R. Stark, MC
Robert S. Goldsmith, MD
Vernon Juchau, PhD
COL Creed Smith, MSC
Samuel Donta, MD
Alex Stalcup, MD

INTRODUCTION

The emergency medical care of unattended infants is an unusual event. The airlift of 985 orphans to San Francisco following the collapse of the South Vietnamese government afforded an opportunity to study the health problems and to appraise the management of large numbers of very young institutionalized children. Before the children arrived, it was necessary to plan what facilities would be used, how major illnesses would be treated, and how the volunteer staff could be protected against infectious diseases the children might carry. As the operation progressed, more effective health care facilities became logistically possible, and we were able to evaluate which of the three facilities most effectively curtailed the transmission of disease to health care workers. Our data indicate a massive infant-to-adult transmission of short-incubation diarrhea due to enteropathogenic Escherichia coli (EEC).

MATERIALS AND METHODS

During a two-week period in April 1975, approximately 5,000 adults (4,000 civilians and 1,000 military and civilian post personnel) at the Presidio Army Base in San Francisco provided medical care for 985 infants and young children airlifted from Saigon in a series of six flights (Figs. 1 and 2). Nearly half the children were under two years and only a few were over seven years old.

During the first eight days of the airlift, three medical care facilities were successively developed (Figs. 1

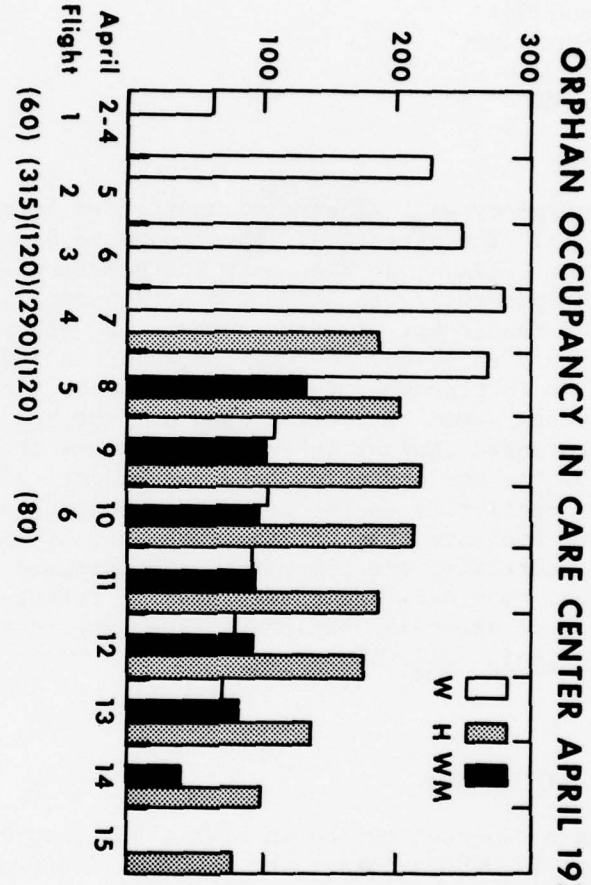
ORPHAN OCCUPANCY IN CARE CENTER APRIL 1975
300
200
100
W H WM
April 2-4 5 6 7 8 9 10 11 12 13 14 15
Flight 1 2 3 4 5 6
(60) (315)(120)(290)(120) (80)

Figure 1

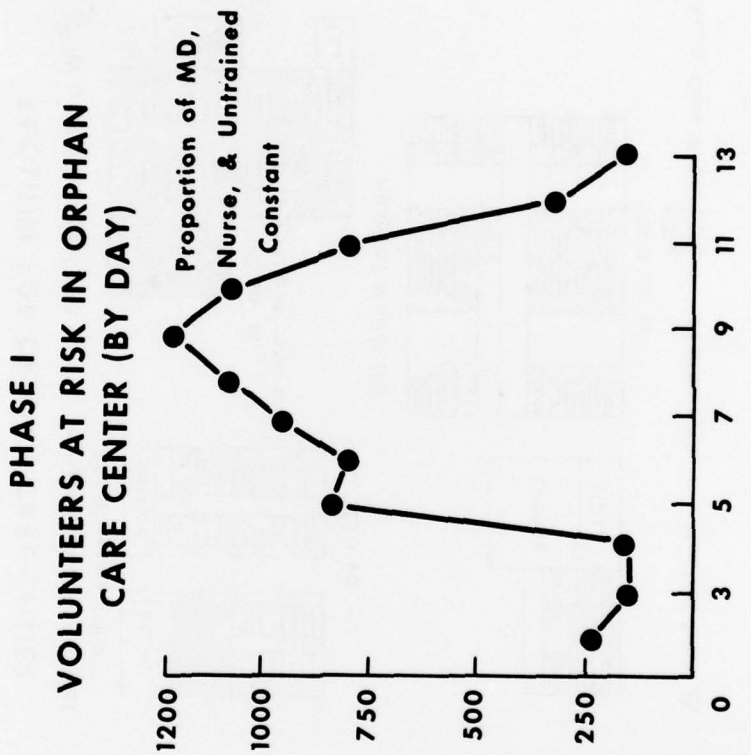
PHASE I
VOLUNTEERS AT RISK IN ORPHAN
CARE CENTER (BY DAY)
Proportion of MD,
Nurse, & Untrained
Constant
1200
1000
750
500
250
0
3
5
7
9
11
13

Figure 2

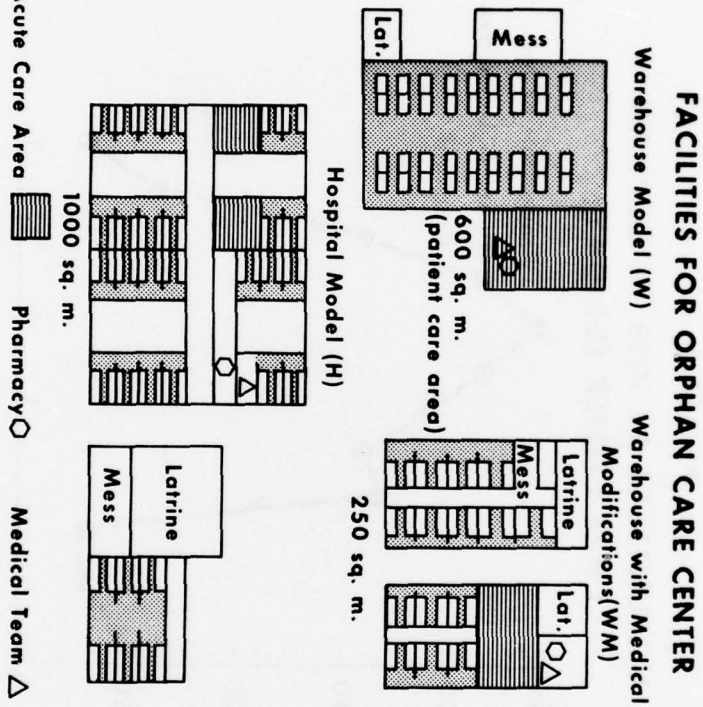
FACILITIES FOR ORPHAN CARE CENTER
Warehouse Model (W)
Lat.
Mess
600 sq. m.
(patient care area)
Warehouse with Medical Modifications(WM)
Latrine
Mess
250 sq. m.
Lat.
Hospital Model (H)
1000 sq. m.
Latrine
Mess
Acute Care Area
Pharmacy
Medical Team

Figure 3

and 3). The first facility, the "warehouse" (W) type was a large open room in an armory. It provided approximately 2.0 square meters of space for each child; however, the number of gowns and hand-washing facilities was limited and there was no isolation area. Nearly 300 persons worked in this care area during each eight-hour shift. Volunteers, most of them untrained, cared for the infants on a one-to-one basis; initially, one professional person supervised 10 volunteers, but this staffing ratio improved over time.

As more supplies became available and military personnel were formally directed to assist, the second facility, the "warehouse with medical modifications" (WM), was developed. This facility provided 2.5 square meters of space for each child, with four to 20 children in each room, and adequate hand-washing and gowning facilities for personnel, but no isolation room. Nearly all of the 125 personnel who worked eight-hour shifts in WM were medically trained (advanced military corpsmen, nurses and physicians). The child-to-staff ratio was 2.5 to 5.0, considerably higher than in W. The ratio of nonprofessional to professional staff was about 1 to 10.

The third facility, the "hospital" (H), provided 5.0 square meters of space for each child (one or two children per room), adequate hand-washing and gowning facilities, and an isolation room for severely ill patients. The child-to-staff ratio was 2.5 to 5.0 and approximately half of the staff members were health professionals. The isolation area was staffed only by trained medical personnel.

The volunteers were taught how to maintain proper personal hygiene in crowded conditions and received instruction on infant and child care.

Logistic limitations, like the shortage of gowns, were rapidly corrected. Because hand-washing facilities were inadequate in W, hand basins containing povidone-iodine solution were provided at a ratio of one basin for every 10 children. The solution was replaced hourly. In addition, the workers were instructed to wash their hands in sink basins before meals and upon leaving W. Hand basins were not provided in the other facilities because they had sufficient sink basins.

Approximately 1,500 persons--198 of 250 San Francisco State University student volunteers and over 1,200 of 2,400 Presidio personnel (military and civilian)--were asked to complete questionnaires about details of their health in the two to three week period following the airlift. Of the 1,400 questionnaires returned, 1,267 included sufficient information from persons who had been exposed to children in one of the three medical care units. We used responses of approximately 5% of workers in W, 50% in WM, and 20% in H. We compared these responses with monthly disease incidence at the Presidio, the military post records for sick call, and the emergency room admissions at Letterman Army Medical Center (LAMC) for February to May 1975 (Figs. 4 and 5).

Serving as controls in this study were 743 persons (military and civilian) who worked at the Presidio but who had no contact with care facility buildings, food served in the buildings, or the children.

Detailed clinical records maintained for most infants and children formed the basis for calculations of disease incidence. Stool specimens were obtained for bacteriologic culture from 367 children (mostly under 18 months of age) within 72 hours after their arrival at the facility, and from 198 student volunteers and 74 army corpsmen within 7 to 10 days after their exposure to the children. /1/ Of these 272 adults, 48% had diarrhea. The specimens were processed by standard methods. Escherichia coli was identified from two to four randomly chosen outgrowths of each stool specimen.

Only E. coli isolates positive by serologic tests were further tested by biologic methods. Tests for enterotoxicity were carried out by the adrenal cell /2/ and infant mouse intestinal tests /3/. Studies for invasiveness were carried out by the Sereny guinea pig eye test. /4/

RESULTS

DESCRIPTION OF DISEASE AND COURSE OF EPIDEMIC

The major clinical findings for the 692 children at the care center were diarrhea (32%), otitis media (28%), upper

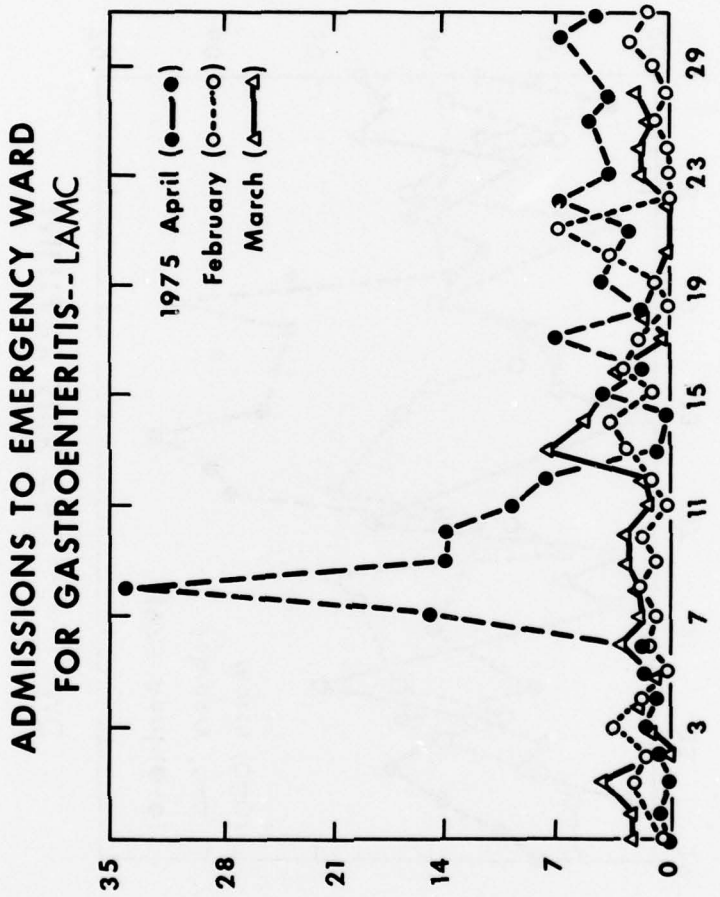
ADMISSIONS TO EMERGENCY WARD
FOR GASTROENTERITIS-- LAMC
1975 April (●—●)
February (○---○)
March (△—△)
35
28
21
14
7
0
3
7
11
15
19
23
29

Figure 4

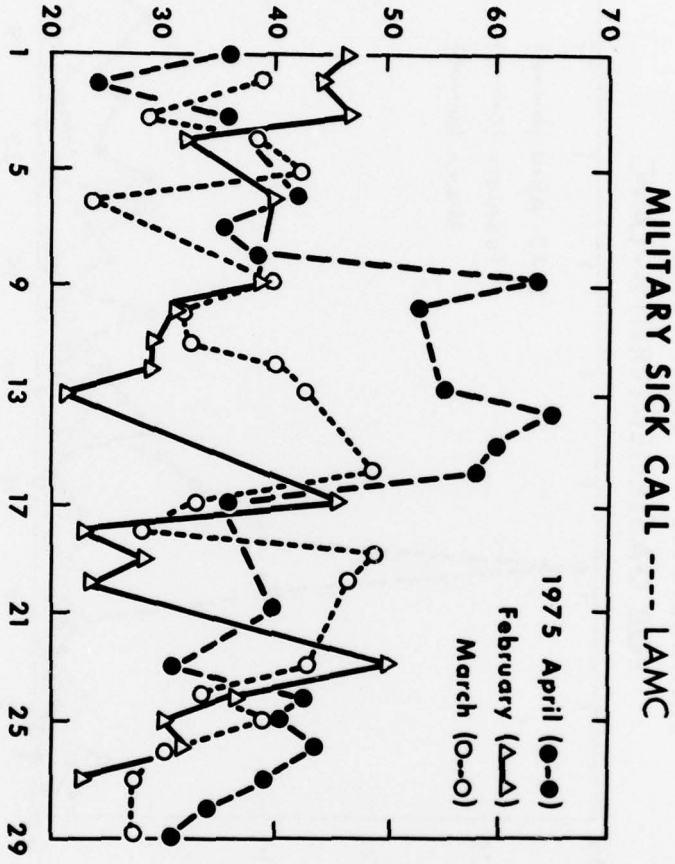
MILITARY SICK CALL ---- LAMC
1975 April (●-●)
February (Δ-Δ)
March (O--O)
70
60
50
40
30
20
1
5
9
13
17
21
25
29

Figure 5

respiratory tract signs (24%), hepatosplenomegaly (22%), fever (18%), conjunctivitis (16%), and varicella (1%). Mild to severe skin infections and scabies were common.

Adults suffered an illness characterized by temperature to 39 C, chills, diarrhea, abdominal cramps and (rarely) vomiting. The syndrome usually began three to six days after the first exposure to the children, had an abrupt onset, and lasted for one to three days. Approximately 16% of the adults also had upper respiratory symptoms; throat washings for viral studies on six subjects yielded no isolate. The course of the outbreak of diarrhea in the 272 adults from whom stool cultures were obtained is presented in Fig. 6.

The outbreak of gastrointestinal disease among adults is reflected in the LAMC emergency ward admissions, records for gastroenteritis from February through April 1975, and military sick calls for the same period (Figs. 4 and 5). Analysis of the epidemic increase in sick calls showed most patients had gastrointestinal symptoms. The outbreak started three days after the arrival of the first group of children, reached a peak between eight to 14 days, and then gradually declined. Based on an analysis of post-medical records through June, and on the results of the questionnaire, there was no evidence of an outbreak of secondary cases, despite the close contact of a large number of persons who lived together in army barracks.

BACTERIAL ISOLATES FROM STOOL SPECIMENS

The following were isolated from the 367 stool specimens from the children: 16 (4.3%) Shigella; 15 (4.1%) Salmonella; 161 (43.8%) seropositive Escherichia coli; 7 (1.9%) Edwardsiella; 2 (0.5%) Versinia pseudotuberculosis; and one (0.3%) Arizona. The Shigella serotypes were: 3 dysenteriae (2 type 7, 1 untyped); 8 flexneri and 5 sonnei. The Salmonella bioserotypes were: 6 S. senftenberg; one each ughelli, kristianstad, lanka, mundsburg, agona, montevideo, havana and group E_2 not typable further, and one not typable. The E. Coli serogroups were 20 group A, 32 B, 71 C, 9 D, and 29 E.

The following isolations were made from the stool specimens from the 198 student volunteers and the 74 corpsmen: 1 Salmonella; 3 Shigella, and 105 seropositive E. coli (2 group A; 8 B; 19 C; 19 D; and 57 E) strains.

When processed in the bioassay tests, the following results were obtained for the 266 seropositive E. coli isolated from both adults and children: 12 (5%) were positive by Sereny test, 63 (24%) were positive by mouse intestinal test, and two (1%) by adrenal cell test. Because so few were positive by adrenal cell test, they were not included in the analysis that follows. All bioassays were performed between August 1975 and May 1976. Replicate tests showed some variation in results, especially a decline in activity in the mouse test of strains stored at 4° C during this period. Unfortunately, none of the seronegative E. coli isolates were saved in order that they also could be tested by biologic test methods.

ASSOCIATION BETWEEN DIARRHEA AND ENTEROPATHOGENICITY OF THE E. COLI ISOLATES

Table shows the association between diarrhea and enteropathogenicity of the seropositive E. coli as determined by biologic testing of the isolates. Diarrhea occurred in 58 of 69 persons (84%) (adults and children) who excreted seropositive E. coli that were also biotest positive by mouse or Sereny tests, or both. This contrasts with diarrhea occurring in only 31 of 157 persons (20%) who excreted seropositive E. coli that were negative in the biologic tests (S.E. = 5.9, $p < 0.00$.). When the data for infants and adults are looked at separately, the same magnitude of differences in diarrheal rates are found.

When biologic test results were not considered in comparing the frequency of diarrhea among subjects (adults and children combined) the findings were not significant. The frequency rates of diarrhea for those whose specimens yielding seropositive E. coli, and those yielding seronegative E. coli, were 39% and 41%, respectively ($p < 0.02$). When the data for adults and infants are looked at separately, there again are no significant differences in diarrheal rates between the seropositive and seronegative groups.

TABLE
ASSOCIATION BETWEEN DIARRHEA IN INFANTS AND STAFF
AND ENTEROPATHOGENICITY OF THE SEROPOSITIVE ISOLATES
AS DETERMINED BY BIOLOGIC TESTING* OF THE ISOLATES

Serologic Test Results	Biologic* Test Results	Infants		Staff		Infants & Staff	
		No. With Diarrhea / No. Tested	% With Diarrhea	No. With Diarrhea / No. Tested	% With Diarrhea	No. With Diarrhea / No. Tested	% With Diarrhea
Positive	Positive	27/ 31	87	31/ 38	82	58/ 69	84
Positive	Negative	24/ 92	26	7/ 65	11	31/157	20
Subtotal		51/123	41	38/103	37	89/226	39
Negative	Not tested	33/103	32	93/202	46	126/305	41
Total		84/226	37	131/305	43	–	–

* By mouse and/or Sereny test.

DIARRHEAL ATTACK RATES FOR STAFF AND INFANTS BY MEDICAL FACILITY AND BY SEROLOGIC AND BIOLOGIC TEST CHARACTERISTICS OF THE E. COLI ISOLATES

In facility W, 195 of about 250 student volunteers provided stool specimens. Sixty-five specimens yielded seropositive E. coli and 130 yielded seronegative E. coli. The diarrheal rates in the two groups were 55% and 46%, respectively. Among the seropositive E. coli isolates, diarrhea was associated with 22 of 29 (76%) specimens positive in the biologic tests, but with only 4 of 36 (11%) specimens negative in these tests. (Fisher two-tailed test $p < 0.05$). Eighty-seven of about 500 infants in facility W provided stool specimens; 42 yielded seropositive E. coli, 45 seronegative E. coli, and diarrheal rates were 45% and 33%, respectively. Among the seropositive E. coli isolates, diarrhea was associated with nine of 11 (82%) of specimens positive in the biologic tests, and with 10 of 31 (32%) negative in these tests. These results were not significant ($p = 0.75$).

In the WM facility, 100 of approximately 125 staff members provided stool specimens; 38 yielded seropositive E. coli, 62 seronegative E. coli, and diarrheal rates were 32% and 53%, respectively. Among the seropositive E. coli isolates, diarrhea was associated with all of nine specimens positive in the biologic tests, but with only three of 29 (10%) negative in these tests ($p < 0.05$). Thirty-one of 150 infants in facility WM provided stool specimens; 18 yielded seropositive E. coli, 13 seronegative E. coli, and diarrheal rates were 67% and 23%, respectively. Among the seropositive E. coli isolates, diarrhea was associated with 11 of 12 (92%) specimens positive in the biologic test, but with only one of six (17%) negative in these tests ($p > 0.20$).

In facility H, 10 of about 500 staff members provided stool specimens; all 10 yielded seronegative E. coli. One hundred and eight of 250 infants in facility H provided specimens; 63 yielded seropositive E. coli, 45 seronegative E. coli, and diarrheal rates were 32% and 33%, respectively. Among the seropositive E. coli isolates, diarrhea was associated with seven of eight (87%) specimens positive in the biologic tests, but with only 13 of 55 (24%) negative in these tests.

DISCUSSION

Traveler's diarrhea (turista) is a mild to moderate, self-limited episode of diarrhea, malaise, and (sometimes) fever that occurs frequently in travelers visiting foreign countries. Although its etiology is not established, probably a large proportion of cases are caused by invasive or enterotoxin-producing E. coli. /7/ In our "experiment" which took place as a result of an airlift, roles were reversed: the immigrant children acted as the endogenous population and the volunteer health workers were the equivalent of "tourists."

An outbreak of both diarrhea (attack rate of 34%) and upper respiratory illness (16%) occurred among the volunteers. The diarrhea was short-lasting and mild, but resulted in marked increases in sick call visits at the military post (Fig. 5) and emergency room admissions at LAMC (Fig. 4). Further evidence that infectious agents were transmitted from children to adults comes from an analysis of the outbreak of diarrhea in the 272 volunteers; isolates from their stool specimens include 105 seropositive E. coli (12 that show invasiveness and 63 enterotoxicity) plus 3 Shigella and 1 Salmonella strains. The children had the same array of enteric isolates and pathogens, although in different proportions.

This study supports the view of others that pathogenicity of E. coli is not related to serotyping /8/ but to virulence factors such as the ability of a strain to produce toxin, to be invasive, or to have an "adhesive" property /9/. An attack rate of 26% among adults and children excreting seropositive E. coli, contrasted with a rate of 41% among persons excreting seronegative E. coli.

The correlation of diarrhea with the bioassay status of the E. coli isolates was strong: 84% of persons excreting seropositive, biologic test-positive organisms had diarrhea, but only 20% of those excreting seropositive, biologic test-negative organisms had diarrhea.

The explanation is not clear for the high rate of diarrhea among two groups, the seropositive, biologic test-negative group, and the seronegative group. The seronegative E. coli isolates were not tested in the biologic tests, yet some isolates probably had virulence factors that were responsible for the diarrhea. Other workers /9/ have demonstrated that serotype negative E. coli may be enteropathogenic because they produce enterotoxins or because they have the capacity to be invasive. Salmonella and Shigella infections were undoubtedly responsible for a small percentage of the infections. Viral etiologies were not adequately excluded. The viral isolations attempted from stools of a few hospitalized patients were unsuccessful; stools were not checked for viral agents by electron microscopy. /10/ In addition, because some E. coli strains tested by biologic methods had been stored for some time, they may have lost toxigenicity as they aged. /11/

The paucity of literature on infant care in an emergency was discussed in our previous publication. /1/ In this study, high levels of sanitation, space, and professional care substantially modified the attack rates for gastrointestinal symptoms for the three facilities: W, 44%; WM, 45%; and H, 23%. Analysis of our findings shows that disease acquisition was high in W, a large open room, where there was a low level of professional care, initially inadequate handwashing and gowning facilities, and no isolation facilities. Even with some medical modifications and improved professional staffing in facility WM, the attack rate did not improve. Transmission rates did not decrease until the H facility was used in which infants with explosive diarrhea were isolated, sufficient space per infant was allocated, full handwashing and gowning facilities appropriate to a hospital were available, and a large professional staff was used.

We suggest in the event of future comparable emergencies that a high ratio of professional/nonprofessional staff be reached (greater than 50%) and that the overall health care worker/infant ratio be at most 1 to 5. A separate full isolation facility (or hospital backup) should be available. No less than 5.0 m^2 of space should be allocated per child; preferably, 10 m^2, as recommended for newborns by the American Adacemy of Pediatricians for neonates. In addition,

adequate stockpiles of gowns, masks, gloves, formulas, and other supplies are needed. In the United States, the best facilities would appear to be hotels or motels that have many rooms, rather than a large open room such as a local gymnasium or armory.

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